Amendments to the Specification:

Please amend the specification as shown:

Please delete the table bridging page 15 and page 16, and replace it with the following table:

Genes		Targeted sequences (5'-3')	Notes
mVEGF-A	1	AAGCCGTCCTGTGTGCCGCTG **(SEQ ID NO: 1)**	91-111 nt of cds, or 151-171 or XM_192823 sequence.
	2	AACGATGAAGCCCTGGAGTGC **(SEQ ID NO: 2)**	133-153 nt of cds, or 193-213 nt of XM_192823 sequence.
mVEGFR-1	1	AAGTTAAAAGTGCCTGAACTG **(SEQ ID NO: 3)**	82-102 nt of cds, or 333-353 nt of D88689
	2	AAGCAGGCCAGACTCTCTTTC **(SEQ ID NO: 4)**	131-151 nt of cds, or 382-403 nt of D88689
mVEGFR-2	1	AAGCTCAGCACACAGAAAGAC **(SEQ ID NO: 5)**	97-117 nt of cds, or 304-324 nt of NM_010612
	2	AATGCGGCGGTGGTGACAGTA **(SEQ ID NO: 6)**	233-243 nt of cds, or 440-460 nt of NM_010612

Please delete the paragraph on page 24, line 29 to page 25, line 12 and replace it with the following paragraph:

The ocular stromal keratitis (SK) BALB/c mouse models were previously reported where cornea NV was induced either by CpG DNA oligo (CpG ODN), that contained the equivalent NV-inducing motif in HSV DNA genome, implanted into stroma through micropocketing procedure, or by HSV-1 viral infection through corneal scarification. The

sequences of stimulatory ODNs used in this study were: 1466, TCAACGTTGA **(SEQ ID NO: 7)**, and 1555, GCTAGA CGTTAGCGT **(SEQ ID NO: 8)** (provided by Dr. Dennis M. Klinman, Biologics Evaluation and Research, FDA, U.S.A.). The pellet to be used for implantation into the corneal micropocket contained an equal molar mixture of ODNs 1466 and 1555, along with hydron polymer as reported previously. HSV-1 strain RE (by Dr. Robert Lausch, Uni. Alabama, Mobile) was used in the induction of HSK at the dosage of $1x10^5$ plaque-forming units per eye in a 2-μl value. To test the *in vitro* RNAi effect, the following three cell lines were used: RAW264.7 gamma NO (-), ATCC, CRL-2278, a mouse macrophage cell line, expressing endogenous mVEGF-A. SVR, ATCC CRL-2280, a mouse endothelial cell line bearing receptors for mVEGF (mVEGFR1 and mVEGFR2). 293 cell line, to be transfected with plasmid pCImVEGFR2 expressing mVEGFR2 driven by cmv promoter, for the detection of the knockdown of exogenous mVEGFR2.

Please delete the paragraph on page 25, line 15 to line 33 and replace it with the following paragraph:

Double-stranded siRNAs were designed to target the VEGF-pathway factors: mVEGF-A (XM_192823), mVEGFR1 (D88689), and mVEGFR-2 (MN_010612). Two target sequences were picked up from each gene. These sequences are (from 5' to 3'): mVEGF-A 1): AAG CCGTCCTGTGTGCCGCTG **(SEQ ID NO: 1)**; mVEGF-A 2): AACGATGAAGCCCTGGAGTGC **(SEQ ID NO: 2)**; mVEGFR1 1): AAGTTAA AAGTGCCTGAACTG **(SEQ ID NO: 3)**; mVEGFR1 2): AAGCAGGCCAGACTCTCTTTC **(SEQ ID NO: 4)**; mVEGFR2 1): AAGCTCAGCAC ACAGAAAGAC **(SEQ ID NO: 5)**; 2): AATGCGGCGGT GGTGACAGTA **(SEQ ID NO: 6)**. For synthesis of unrelated siRNA

controls, two target sequences each for LacZ (E00696) and firefly luciferase (Luc, AF434924) were also selected. They were: LacZ 1): AACAGTTGCGCAGCCTGAATG **(SEQ ID NO: 9)**; LacZ 2): AACTTAATCGCCTTGCAGCAC **(SEQ ID NO: 10)**; Luc 1): AA GCTATGAAACGATATGGGC **(SEQ ID NO: 11)**; 2): AACCGCTGGAGAGCAACTGCA **(SEQ ID NO: 12)**. Blast sequence searching confirmed the specificity of these siRNAs with their targeted sequences, and the mVEGF-A targets were designed to be shared by different mVEGF-A isomers. All siRNAs were custom-designed as 21-nt double stranded RNA oligos with 19-nt duplex in the middle and dTdT overhang at the 3'-end of either RNA strand, following the well-accepted guidelines proposed by Tuschl's group; and were synthesized by Qiagen. To get better RNAi effect, we routinely used a mixture of two double-stranded 21-nucleotide RNA duplexes targeting two different sequences on a single mRNA molecule.

Please delete the paragraphs on page 26, line 2 to line 29 and replace it with the following paragraphs:

The RS-PCR was performed for detection of mRNA knockdown by siRNAs in vitro. Cytoplasmic RNA was isolated by RNAwiz (Ambion, #9736) according to the manufacturer's instruction with additional DNAse treatment, and subjected to RS-PCR with specially designed primers. The mRNA-specific reverse primers for the RT reaction were all 47-mer oligos with the 5'-end 30-mer of unique sequence (called "TS1" sequence, indicated in uppercase below) linked to a 17-mer sequence unique for each mRNA molecule (in lower case below). They were (from 5' to 3'):

1) mVEGFA Dn:

GAACATCGATGACAAGCTTAGGTATCGATAcaagctgcctcgccttg **(SEQ ID NO: 13)**;

2): mVEGFR1 Dn: GAACA

TCGATGACAAGCTTAGGTATCGATAtagattgaagattccgc **(SEQ ID NO: 14)**;

3) mVEGFR2 Dn: GAACATCGATGACAAGCTT

AGGTATCGATAggtcactgacagaggcg **(SEQ ID NO: 15)**.

The PCR assays for all the tested genes, that follow the RT assay, used the same reverse primer, TS1: GAACATC GATGACAAGCTTAGGTATCGATA **(SEQ ID NO: 16)**. The forward primers for PCR, were 30-mer oligos, unique for each gene:

1) mVEGFA Up: GATGTCTACCAGCGAA GCTACTGCCGTCCG

(SEQ ID NO: 17);

2) mVEGFR1 Up: GTCAGCTGC TGGGACACCGCGGTCTTGCCT

(SEQ ID NO: 18);

3) mVEGFR2 Up: GGCGCTGCTAGCTGTCGCTCTGTGGT TCTG

(SEQ ID NO: 19).

The RT-PCR of the housekeeping gene GAPDH was used as a control for the RNA amount used in RS-PCR. An oligo dT primer (19-mer) was used for RT assay of GAPDH. The primers used for the PCR were 20-mer oligos:

1) GAPDH Up: CCTGGTCACCA GGGCTGCTT **(SEQ ID NO: 20)**;

2) GAPDH Dn: CCAGCCTTCTCCATGGTGGT **(SEQ ID NO: 21)**.

RT-PCR was also used according to protocol described previously. For the detection of mVEGF-A expression the primers used were 5'-GCGGGCTGCCTCGC AGTC-3'

(SEQ ID NO: 22) (sense) and 5'-TCACCGCCTTGGCTTGTCAC-3' **(SEQ ID NO: 23)** (antisense).

Please delete the paragraph on page 26, line 32 to page 27, line 14 and replace it with the following paragraph:

QRT-PCR was performed using a DNA Engine Opticon (MJ Research Inc.). PCR was performed using SYBR Green I reagent (Qiagen, CA), according to the manufacturer's protocol. During the optimization procedures of the primers, 1% agarose gel analysis verified the amplification of one product of the predicted size with no primer-dimer bands. The absence of primer-dimer formation for each oligonucleotide set was also validated by establishing the melting curve profile. The semi-quantitative comparison between samples was calculated as follows: the data were normalized by subtracting the difference of the threshold cycles (C_T) between the gene of interest's C_T and the "housekeeping" gene GAPDH's C_T (gene of interest C_T – GAPDH $C_T = \Delta C_T$) for each sample. The ΔC_T was then compared to the expression levels of the vector control sample (sample ΔC_T – vector ΔC_T). To determine the relative enhanced expression of the gene of interest, the following calculation was made: fold change = $2^{(-\text{ sample } \Delta CT - \text{ vector } \Delta CT)}$. The primers used were mGAPDH sense, 5'-CATCCTGCACCACCAACTGCTTAG-3' **(SEQ ID NO: 24)** and GAPDH antisense, 5'-GCCTGCTTCACCACCTTCTTGATG-3' **(SEQ ID NO: 25)**, mVEGF164 sense, GCCAGCACATA GAGAGAATGAGC **(SEQ ID NO: 26)** and mVEGGF165 antisense, CAAGGCTCACA GTGATTTTCTGG **(SEQ ID NO: 27)**.

Please delete the paragraph on page 27, line 17 to line 29 and replace it with the following paragraph:

PolyTran™ (PT) and TargeTran™ (TT), were used for local and systemic delivery of siRNAs, through subconjuctival and tail vein infection, respectively. PT is a class of cationic polypeptides that transformed cells at high efficiency by the positively charged particle surface. TT belongs to ligand-targeted nanoplex with greatly reduced nonspecific interaction with unwanted biomolecules and cells. TT consists of three functional layers: a RGD ligand of peptide H-ACRGDMFGCA-OH **(SEQ ID NO: 28)** that was structurally similar to the previously reported RGD-containing peptides, a PEG steric layer, and a cationic PEI core that concentrate siRNA or other macromolecules (Fig. 1). By design, the TT-siRNA formulation targets the angiogenic tissue where the RGD-specific intergrins are up-regulated. The efficacy of TT-siRNA formulation has been proven in a previous study in a xenograft breast cancer mouse tumor model where the delivery of siRNAs targeting human VEGF and mouse VEGFR2 achieved substantial inhibitory effect on tumor growth.

Please delete the paragraph on page 35, line 5 to line 17 and replace it with the following paragraph:

Short double stranded RNA oligonucleotides for siRNA labeled siLuc, siLacZ, siGFP, and siVEGFR2 were designed based on studies by Elbashir et al. (2), validated to lack significant interfering homology by BLAST-analysis, and synthesized and purified by Dharmacon (Lafayette, CO). Two sequences were synthesized per target and combined in a 1:1 molar ratio. Target sequences used were for siLuc: aaccgctggagagcaactgca **(SEQ ID NO: 12)**

and aagctatgaaacgatatgggc **(SEQ ID NO: 11)**, for siLacZ: aacagttgcgcagcctgaatg **(SEQ ID NO: 9)** and aacttaatcgccttgcagcac **(SEQ ID NO: 10)**, for siGFP: aagctgaccctgaagttcatc **(SEQ ID NO: 29)** and aagcagcacgacttcttcaag **(SEQ ID NO: 30)** and for siVEGFR2: aatgcggcggtggtgacagta **(SEQ ID NO: 6)** and aagctcagcacacagaaagac **(SEQ ID NO: 5)** (inhibition of VEGF R2 by this siRNA has been described (28)). siRNA targeted against luciferase was labeled with fluorescein (FITC-siRNA) at the 3' position of the sense strand with standard linkage chemical conjugation, for FACS-analysis and tissue distribution experiments. The luciferase-encoding pCI-Luc plasmid (pLuc) was obtained from Lofstrand Labs (Gaithersburg, MD).

Please delete the paragraph on page 35, line 23 to line 27 and replace it with the following paragraph:

The cyclic 10-mer RGD-peptide with the sequence H-ACRGDMFGCA-OH **(SEQ ID NO: 28)**, was synthesized, oxidized to form an intramolecular disulfide bridge and purified to >95% purity by Advanced ChemTech (Louisville, KY, USA). This sequence was derived from the integrin binding RGD peptides identified by phage display and has been found effective for cell binding and internalization (23,29).

Please delete the paragraph on page 42, line 21 to line 23 and replace it with the following paragraph:

The siRNA agents are designed and prepared following methods of the invention and as illustrated in Example 1. The sequences of suitable siRNA agents are shown in Appendix II below **(SEQ ID NOS 31-374, respectively in order of appearance)**.

Please delete the paragraph on page 43, line 19 to page 44, line 21 and replace it with the following paragraph:

For mVEGF-A (reference sequence: XM_192823)

Primer 1: mVEGF-A Up (30-mer, 4-33 nt of mVEGF-A coding sequence, or 64-93 nt of cloning sequence).

5'---GAT GTC TAC CAG CGA AGC TAC TGC CGT CCG---3' **(SEQ ID NO: 17)**

Primer 2: mVEGF-A Dn (47-mer, the first 30 is the same as "TS1 primer", the following 17-mer is complementary to the 403-387 nt of mVEGF-A coding sequence, or 463-447 nt of cloning sequence).

5'---GAA CAT CGA TGA CAA GCT TAG GTA TCG ATA caa gct gcc tcg cct tg ---3' **(SEQ ID NO: 13)**

For mVEGFR-1 (reference sequence: D88689)

Primer 3: mVEGFR-1 Up (30-mer, 4-33 bp of mVEGFR-1 coding sequence, or 255-284 of cloning sequence)

5'--- GTC AGC TGC TGG GAC ACC GCG GTC TTG CCT ---3' **(SEQ ID NO: 18)**

Primer 4: mVEGFR-1 Dn (47-mer, the first 30 is the same as "TS1 primer", the following 17-mer is complementary to the 377-361 nt of mVEGFR-1 coding sequence, or 628-612 nt of cloning sequence).

5'---GAA CAT CGA TGA CAA GCT TAG GTA TCG ATA tag att gaa gat tcc gc---3' **(SEQ ID NO: 14)**

For mVEGFR-2 (reference sequence: D88689)

Primer 5: mVEGFR2/400Dn (47-mer, 3' 17-mer complementary to mVEGFR2 400-384 nt)

5'--- GAA CAT CGA TGA CAA GCT TAG GTA TCG ATA ggt cac tga cag agg cg---3' **(SEQ ID NO: 15)**

Primer 6: mVEGFR2/12up (30 –mer, 12-41 of mVEGFR2)

5'---GGC GCT GCT AGC TGT CGC TCT GTG GTT CTG---3' **(SEQ ID NO: 19)**